

Surgery for Acquired Cardiovascular Disease

Ross operation: 16-year experience

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Objective: We performed a review of a consecutive series of 487 patients undergoing the Ross operation to identify surgical techniques and clinical parameters that affect outcome.

Methods: We performed a prospective review of consecutive patients from August 1986 through June 2002 and follow-up through August 2004. Patient age was 2 days to 62 years (median, 24 years), and 197 patients were less than 18 years of age. The Ross operation was performed as a scalloped subcoronary implant in 26 patients, an inclusion cylinder in 54 patients, root replacement in 392 patients, and root–Konno procedure in 15 patients. Clinical follow-up in 96% and echocardiographic evaluation in 77% were performed within 2 years of closure.

Results: Actuarial survival was $82\% \pm 6\%$ at 16 years, and hospital mortality was 3.9%. Freedom from autograft failure (autograft reoperation and valve-related death) was $74\% \pm 5\%$. Male sex and primary diagnosis of aortic insufficiency (no prior aortic stenosis) were significantly associated with autograft failure by means of multivariate analysis. Freedom from autograft valve replacement was $80\% \pm 5\%$. Freedom from endocarditis was $95\% \pm 2\%$. One late thromboembolic episode occurred. Freedom from allograft reoperation or reintervention was $82\% \pm 4\%$. Freedom from all valve-related events was $63\% \pm 6\%$. In children survival was $84\% \pm 8\%$, and freedom from autograft valve failure was $83\% \pm 6\%$.

Conclusions: The Ross operation provides excellent survival in adults and children willing to accept a risk of reoperation. Male sex and a primary diagnosis of aortic insufficiency had a negative effect on late results.

Dissatisfaction with available options for aortic valve replacement in children and young adults led us to initiate the use of the Ross operation in August 1986. Clinical evaluation and echocardiographic surveillance at completion of the operation, 3 months postoperatively, 6 months postoperatively, and annually thereafter was planned. Although the initial operations were done as scalloped subcoronary implants, we rapidly changed to the modified subcoronary implant or root replacements in selected patients. Subsequent success with the root replacement led to its use in almost all patients. The use of the Ross operation has expanded to patients with complex left ventricular outflow tract obstruction, patients with active endocarditis, and the newborn. Prior reviews of this prospective study identified mechanisms of early failure and led to alterations in the procedure for management of patients with significant aortic insufficiency (AI), aortic annular dilation, and ascending aortic disease.^{1,2}

Abbreviations and Acronyms

AGI	= autograft valve insufficiency
AI	= aortic insufficiency
ALF	= allograft valve failure
AS	= aortic stenosis
BSA	= body surface area
CI	= confidence interval
GEE	= generalized estimating equation
HR	= hazard ratio
VSD	= ventricular septal defect

This article addresses questions about the durability and operative risk of the Ross operation and the preferred operative technique, in particular the risk of progressive dilation of the autograft root and failure of the allograft reconstruction of the right ventricular outflow tract. We report the long-term results at a single institution during the period when use of the Ross operation expanded worldwide and seek to identify operative techniques and patient characteristics associated with survival and autograft valve durability.

Materials and Methods

All 487 patients having a Ross operation at the University of Oklahoma Health Sciences Center between August 1986 and July 2002 were entered into a prospective database, which was queried as of August 2004. Surgeons offered the Ross operation to all children, young adults with isolated aortic valve disease, and older adults with an active lifestyle and a desire to avoid postoperative anticoagulation. Children and young adults with significant abnormalities of the autologous pulmonary valve were not candidates and were managed with allograft aortic valve replacement. Noncandidate adults were managed with a prosthetic valve or an allograft valve based on their choice.

The numbers of Ross operations and of all other aortic valve replacements for each year of the study are shown in Figure E1. Patient characteristics and preoperative clinical information are summarized in Table 1. The autograft valve was inserted as a modified scalloped subcoronary implant in 26 patients, an inclusion cylinder in 54 patients, a root replacement in 392 patients, and a root-Konno procedure in 15 patients. The right ventricular outflow tract was reconstructed with a pulmonary allograft in 484 patients and an aortic allograft in 3 patients for whom a pulmonary allograft was unavailable. Operative findings concerning aortic valve morphology, aortic annulus dilation, or disease of the ascending aorta and management of these abnormalities are listed in Table 2.

Clinical follow-up was obtained by means of annual clinic visits or communication with the referring cardiologist or the patient's personal physician. When physician contact was unavailable, direct communication with the patient or family was attempted. Follow-up was complete within 1 year of the study's closure in 61% of the patients and within 2 years of closure in 96% of the patients. The follow-up represents a total of 3263 patient-years.

Annual echocardiographic surveillance after the first postoperative year was planned. However, with continued follow-up, many patients' physicians elected to obtain echocardiograms every 2 or 3

TABLE 1. Demographics and preoperative clinical information (487 patients)

	n	%
Age: 1 d to 62 y; median, 24 y		
Children: 1 d to 18 y	197	40
Young adults: 18 y to 50 y	251	52
≥50 y	39	8
Sex: 360 male subjects and 127 female subjects; ratio 2.8:1		
Preoperative aortic valve disease		
AI	154	32
AS	91	19
Mixed (AI/AS)	238	49
Other (replacement of normal prosthetic valve)	4	<1
Previous median sternotomy	168	35
Previous aortic valve surgery	162	34
Previous aortic valve replacement	38	8
Aortic balloon valvuloplasty	48	10
Aortic valve endocarditis	40	8
Active	24	5
Primary hemodynamic aortic valve abnormality		
Aortic insufficiency*:		
138 male subjects and 29 female subjects; ratio 4.8:1	167	34
Aortic stenosis:		
222 male subjects and 98 female subjects; ratio 2.3:1	320	66

AI, Aortic insufficiency; AS, aortic stenosis. *Patients with AI without prior history of AS (ie, patient with AI after aortic valvotomy or valvuloplasty classified as AS).

years when their clinical evaluation did not indicate the need for annual assessment. Echocardiograms obtained at the University of Oklahoma Health Sciences Center were reviewed by echocardiographers with a special interest in the patients undergoing the Ross operation. Echocardiograms obtained from outside physicians were reread at the University of Oklahoma Health Sciences Center if they reported significant alteration in autograft or allograft function. Autograft valve insufficiency (AGI) was graded by using the thickness of the regurgitant stream relative to the size of the left ventricular outflow tract³ (0, none or trivial; 1+, mild; 2+, moderate; 3+, moderate-severe; and 4+, severe). Patient migration, loss of health insurance, or both decreased late echocardiographic surveillance. Echocardiographic assessment was available within 2 years of study closure in 2004 in 77% of the patients.

All analyses were performed with SAS System software, version 9.1 (SAS Institute, Inc, Cary, NC). Actuarial survival estimates of freedom from postoperative events were calculated by using Kaplan-Meier method, with differences assessed with the Wilcoxon and log-rank tests. All *P* values are reported. Cox multiple proportional hazards regression analyses were applied to time to autograft valve failure (AGF) and allograft valve failure (ALF).

Two-dimensional echocardiographic measurements of the diameter of the autograft root or autograft sinus (in millimeters) were recorded over time for each patient. Each measurement was

TABLE 2. Operative clinical information for 487 patients

	n	%
Valve morphology		
Congenital bicuspid or unicuspid aortic valve (initial operation)	409	84
Tricuspid aortic valve	78	16
Operative findings		
Aortic annulus dilatation*	167	34
Aneurysm or significant dilation of ascending aorta†	164	34
Operative management		
Aortic annulus reduction and fixation	164	34
Fixation of aortic annulus with synthetic cuff	218	45
Replacement of ascending aorta	100	21
Aortoplasty	60	12
Resection of dilated aorta	4	1

*Aortic annulus diameter greater than predicted diameter by 2 mm. †Aortic z value greater than 2 or diameter greater than 40 mm.

z-transformed by using a regression equation^{4,5} that predicts the mean and standard deviation (root mean square of regression) for the diameter of the aortic sinuses of Valsalva for a given body surface area (BSA). BSAs were calculated by using the technique of Haycock and colleagues.⁶ The z-transformed autograft sinus diameters were subjected to longitudinal analysis in a general linear mixed model that accounted for correlation among an individual's measurements over time. The analysis was restricted to 383 patients who underwent a root replacement, for whom we collected 2147 echocardiographic measurements of root size. The model predicted z-transformed diameters after adjusting for a variety of fixed (between-subject) effects that appear to influence either sinus diameter at the time of surgical intervention or the rate of increase in diameter over time. Effects considered were age, sex, valve morphology, preoperative active endocarditis, primary hemodynamic lesion of aortic stenosis (AS) or AI (no prior AS), ventricular septal defect (VSD; subaortic), coarctation, ascending aortic dilation or aneurysm, prior median sternotomy, prior aortic valve replacement, annular fixation, aortic balloon valvuloplasty, and severity of AGI at completion of the operation. A backward selection technique eliminated variables until those remaining were significant.

Population-average changes in AGI over time were modeled with generalized estimating equations (GEEs) in the 469 operative survivors (3654 echocardiograms). Postoperative observations were truncated at the date of autograft reoperation for 38 patients, 10 of whose reoperations were unrelated to AGI. Predictions were calculated with SAS PROC GENMOD by specifying a cumulative logit model that accounted for repeated observations within subjects. Changes over time in AGI were investigated for the following predictors of outcome: implant technique, age (as a continuous variable), sex, aortic valve morphology, preoperative active endocarditis, primary preoperative hemodynamic lesion of AS or AI (no prior evidence of AS), VSD (subaortic), coarctation, ascending aortic dilation or aneurysm, prior median sternotomy, previous aortic valve replacement, annular fixation, aortic balloon valvuloplasty, and severity of AI at the completion of operation. These variables were entered simultaneously into the longitudinal model and then eliminated one by one until all variables remaining had a *P* value of .1 or less.

Results

Survival

Hospital mortality was 3.9% (19/487). There were 15 late deaths, 7 of which were not cardiac related, 2 of which were valve related, and 6 of which were sudden unexplained deaths counted as valve related. Actuarial survival for all causes was 92% ± 2% at 10 years and 82% ± 6% at 16 years (Figure E2). Actuarial survival from operative or valve-related death was 94% ± 1% and 89% ± 4% at 10 and 16 years, respectively. In patients less than 18 years of age, hospital mortality was 5.6% (11/197). Actuarial survival (all causes) was 92% ± 2% and 84% ± 8% at 10 and 16 years, respectively, and that from all operative and valve-related deaths was 94% ± 2% at both 10 and 16 years. There were no late deaths associated with autograft valve or allograft valve reoperation.

Survival (all causes) among the 487 patients was compared with the survival of the general US population, matched by each patient's age, sex, and year of operation (Figure 1). After the initial decrease associated with early hospital deaths, the survival appears to parallel the survival of the matched population to 13 years. After 13 years, the number of patients available for comparison is less than 10% of the surgical cohort. The confidence limits of the cohort's survival curve widen, limiting the validity of the later comparisons.

Autograft Valve Failure

AGF was defined as autograft valve reoperation or valve-related death. Actuarial freedom from AGF was 86% ± 2% and 74% ± 5% at 10 and 16 years, respectively. Actuarial freedom from AGF in 462 patients (excluding those with an abnormal pulmonary valve or SLE) was 90% ± 2% and 83% ± 5% at 10 and 16 years, respectively. Actuarial freedom from AGF in the 186 children was 88% ± 3% and 83% ± 6% at 10 and 16 years, respectively.

AGF occurred in 46 patients (38 autograft valve reoperations, 2 valve-related deaths, and 6 sudden unexplained

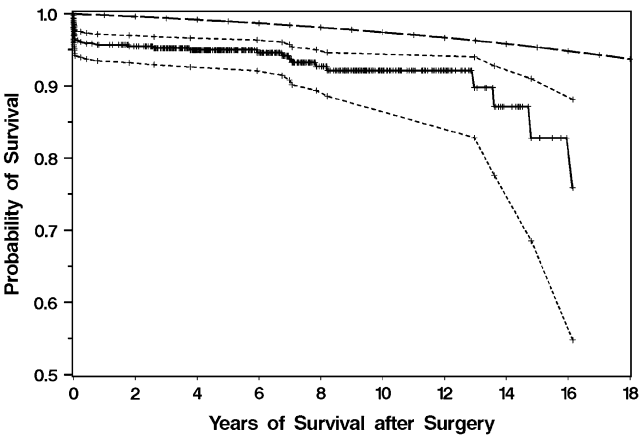


Figure 1. Survival (all causes) among the 487 patients compared with survival of the US population matched for each patient's age, sex, and year of operation.

TABLE 3. Autograft reoperation (38 patients)

By initial operative technique:			
21/389		Root replacements	
12/53		Inclusion cylinder	
5/26		Scalloped subcoronary	
29/409		Bicuspid or unicuspid	
9/78		Tricuspid	
Causes for reoperation			
27	Autograft replacement	Bicuspid	Tricuspid
7	Annulus dilation	4	3
5	Sinus dilation	4	1
5	Endocarditis	3	2
3	Technical	1	2
5	Abnormal pulmonary valve autograft (3 bicuspid, 1 quadricuspid, 1 abnormal commissure)	5	
1	Cusp prolapse	1	
1	Recurrent SLE		1
11	Autograft repair		
7	Annulus dilation		
2	Sinus dilation		
2	Subvalve AS (1 recurrent)		

SLE, Systemic lupus erythematosus; AS, aortic stenosis.

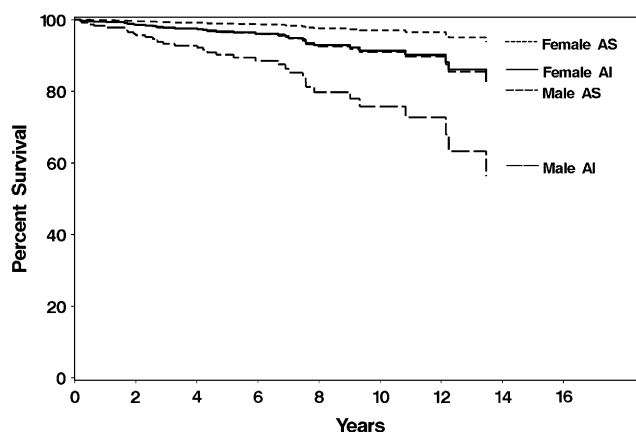
deaths that were counted as valve related). Table 3 identifies the primary causes for AGF requiring reoperation and the incidence of reoperation by initial operative technique. Autograft valve replacement was required in 27 of the 38 autograft valve reoperations, and the actuarial freedom from autograft valve replacement was $90\% \pm 2\%$ and $80\% \pm 5\%$ at 10 and 16 years, respectively.

Univariate Kaplan–Meier analyses identified male sex, primary lesion of AI, and type I VSD as potential risk factors for the development of AGF. Prior aortic valve surgery was protective against AGF. Multivariable analyses with proportional hazards regression confirmed male sex and primary lesion of AI as the only factors associated with an increased risk of AGF (Table 4, A). Predicted freedom from AGF by sex and primary lesion for the proportional hazards model are shown in Figure 2. Patients with primary AI had approximately 3 times the risk for AGF compared with patients

TABLE 4. A. Variables associated with autograft valve failure

Variable	Univariate P value	Hazard ratio (95% CI)	Multivariate P value
Primary lesion, AI	.001	2.9 (1.5–5.7)	.0020
Sex, male	.019	3.1 (1.1–8.8)	.0361
VSD type 1 (subaortic)	.002		

CI, confidence interval; AI, aortic insufficiency; VSD, ventricular septal defect.

**Figure 2. Predicted freedom from autograft failure by sex and for primary lesion for the proportional hazard model.**

with AS, and the risk for male subjects was approximately 3 times that of female subjects.

In 164 patients with primary AI, actuarial freedom from AGF was $59\% \pm 10\%$ at 15 years, which was significantly less than that of 304 patients with AS whose actuarial freedom from AGF was $82\% \pm 6\%$ at 15 years ($P = .02$ Wilcoxon test; $P < .01$, log-rank test). Recognizing the increased incidence of autograft degeneration in patients with AI, we elected in 1995 to institute annulus reduction and fixation in adults and older children with aortic annulus dilation (aortic annulus >27 mm or z value >2 for annulus compared with BSA). Annulus reduction and fixation was used in 96 patients with primary AI, for whom actuarial freedom from AGF was $87\% \pm 8\%$ at 10 years. These results are similar to those of patients with a primary diagnosis of AS (ie, $92\% \pm 2\%$ for the same time period).

Autograft Root Dilation

Figure E3 displays the z-transformed autograft sinus or root diameter for all of the patients (383 operative survivors) who had a root replacement over time. Figure E4 displays mean observed and predicted values (derived from a general linear mixed model) for z-transformed autograft sinus or root diameters in this patient group. Although we planned to perform echocardiographs at specific postoperative intervals, the procedures' actual timing varied considerably. Observations were grouped to use each patient's multiple echocardiographic studies to calculate mean diameters at defined intervals.

The observed baseline (time = 0) mean z value of 1.97 ± 1.88 increases to a z value of 3.15 ± 2.18 at 1 year after the operation. Change thereafter is gradual. A general linear mixed model yielded estimates of aortic diameter that accounted for correlations among patients' repeated measurement over time. The predicted baseline z diameter of 1.96 is adjusted downward by 0.04 z units for each year of a patient's age at the time of the operation. Patients with a primary lesion

of AI have baseline diameters that are 0.57 z units larger ($P = .0026$). Male subjects' baseline diameters are 0.40 z units larger than those of female subjects ($P = .0389$). The cohort included 30 patients with a subaortic VSD, whose diameters were marginally larger (1.35 z units, $P = .058$). No factors were associated with smaller baseline diameters.

The model separately estimated the rate of change in aortic diameter over the first 12 months and after 12 months. Diameter increased by 0.13 z units per month during the first 12 months. The predicted rate of change after 12 months is 0.019 z units per month (standard error, 0.0086; 95% confidence limit, 0.003–0.036).

Four factors were associated with a more rapid increase in diameter over the first 12 months: grade 2 (but not grade 1) baseline AI (an additional increase of 0.18 z units per month, $P = .0249$), bicuspid aortic valve (an additional 0.09 z units per month, $P = .0010$), a history of coarctation (an additional 0.09 z units per month, $P = .0131$), and repair of an aortic aneurysm as part of a Ross operation (an additional 0.06 z units per month, $P = .0047$). After 12 months, these 4 factors were not associated with differences in the overall predicted rate of change of 0.019 z units per month.

Patients who had cuff fixation of their aortic annulus had a rate of change in aortic diameter over the first 12 months that was 0.058 z units per month slower than the others ($P = .0086$). After 12 months, their rate of change was 0.019 z units per month faster than (or about double the rate of those) without cuff fixation ($P = .0005$). We also investigated but found no interaction between sex and primary lesion of AI ($P = .9$) or between the bicuspid aortic valve and aneurysm ($P = .4$) with respect to rate of change in aortic diameter.

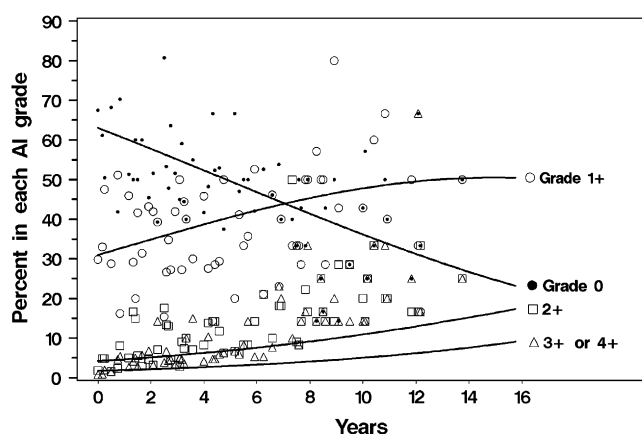


Figure 3. Observed and predicted probabilities of autograft valve insufficiency over time. Predicted percentages of aortic insufficiency (AI) grade (solid line) are obtained from an ordinal longitudinal (generalized estimating equation) model and sum to 100% at a given time of follow-up. The predicted percentage of patients with no AI (grade 0) decreases, whereas other grades gradually increase in time.

Valve Function

Changes over time in the severity of AGI, as observed and predicted by GEEs, are shown in Figure 3. Because few patients had moderate–severe (3+) or severe (4+) AGI, these groups were combined for analysis. The predicted probability of no or trivial (grade 0) AGI decreased from 63% in the early postoperative period to 52% at 5 years, 36% at 10 years, and 24% at 16 years. The predicted probability of mild (grade 1) and moderate (grade 2+) AGI increased, with 50% having mild and 17% having moderate insufficiency at 16 years. A separate GEE analysis that focused only on the development of moderate–severe (3+) and severe (4+) AGI is shown in Figure 4. Predicted 3+ or 4+ AGI slowly increased to 3.3% (70% confidence interval [CI], 2.7%–4%) at 5 years, 7.9% (70% CI, 5.8%–9.5%) at 10 years, and 21.5% (80% CI, 15.3%–29.4%) at 16 years.

Independent variables associated with development of moderate–severe or severe autograft insufficiency were determined by means of GEE analysis. In addition to the time elapsed since the operation, other associated factors were an immediate postoperative AI of grade 1 or higher and the patient's age at the time of the operation. The association of operative technique (intra-aortic implant versus root replacement) was marginal once the other variables were accounted for. Previous aortic valve replacement was associated with a decreased risk of 3+ or 4+ AGI (Table 4, B).

Endocarditis

Actuarial freedom from endocarditis was $95\% \pm 2\%$ at 16 years. Endocarditis occurred in 11 patients; 6 involved the autograft valve, 1 involved the mitral valve, and 4 involved the allograft valve. Autograft valve endocarditis occurred perioperatively in 1 patient, 2.7 years postoperatively in a patient with AGI, and in 4 patients (6 episodes at 4.1–10.1

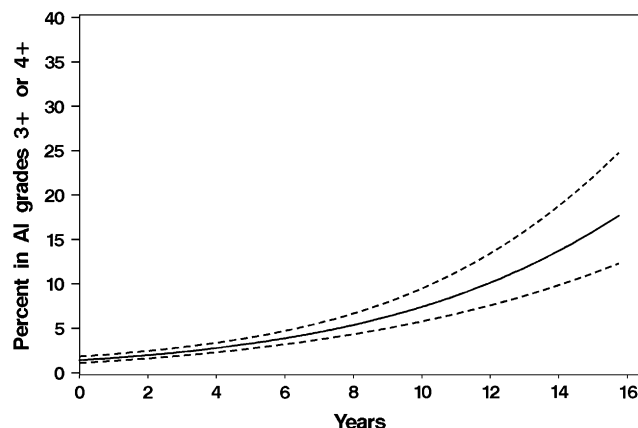


Figure 4. Predicted probabilities of 3+ (moderate–severe) or 4+ (severe) autograft valve insufficiency (AGI) by means of generalized estimating equations over time. AGI slowly increases from 3.3% (70% confidence interval, 2.7%–4%) at 5 years to 21.5% (confidence interval, 15.3%–29.4%) at 16 years.

TABLE 4. B. Variables associated with developing moderate–severe (grade 3) or severe (grade 4) autograft valve insufficiency (according to a GEE model based on cumulative logits)

Variable	Univariate <i>P</i> value	Odds ratio (95% CI)	Multivariable <i>P</i> value
Postoperative AGI, grade 1+ or higher	.003	2.7 (1.2–6.1)	.0176
Intra-aortic implant (vs root replacement)	.0043	2.5 (1.0–6.6)	.0554
Follow-up time (in 1-mo increments)	<.0001	1.01 (1.00–1.02)	.0017
Age (in 1-y increments)	.0255	1.03 (1.01–1.06)	.0088
Previous aortic valve replacement	.0398	0.10 (0.01–0.79)	.029

Previous aortic valve replacement is protective. *GEE*, Generalized estimating equation; *CI*, confidence interval; *AGI*, autograft valve insufficiency.

years) who abused intravenous drugs. Two allograft patients had fungal endocarditis, 1 related to delayed treatment of mediastinitis and 1 after multiple operative procedures for recurrent allograft obstruction. Allograft endocarditis occurred 2.7 years postoperatively as a result of intravenous drug use in 1 patient and 11 years postoperatively in a patient with moderate allograft obstruction.

Thromboembolism

Thromboembolism was identified in only 1 patient who had a nonfatal coronary embolism during treatment for endocarditis. Six patients died suddenly and were presumed to represent valve-related deaths. One or more of these deaths might have been an unrecognized episode of thromboembolism. Anticoagulation was used only in patients who had an associated mitral valve procedure that required anticoagulation.

Allograft Valve Failure

ALF was defined as allograft valve reoperation or intervention. Actuarial freedom from ALF was 90% \pm 2% at 10 years and 82% \pm 4% at 16 years. Multivariable proportional hazard regression identified younger age at operation ($P = .02$; hazard ratio [HR], 0.97; 95% CI, 0.94–0.1), previous aortic valve replacement ($P < .0001$; HR, 6.23; 95% CI, 2.72–14.28), history of bacterial endocarditis ($P = .002$; HR, 4.58; 95% CI, 1.75–11.98), and male sex ($P = .01$; HR, 4.01; 95% CI, 1.39–11.56) as independent risk factors for increased ALF. Allograft valve replacement or intervention was required in 33 patients. Accelerated ALF within 1 year of allograft insertion occurred in 3 patients.

A number of patients with significant obstruction of the allograft conduit or allograft valve insufficiency are being followed. Allograft degeneration was defined as allograft reoperation or intervention, a peak allograft gradient of 50

mm Hg or more, or severe allograft valve insufficiency. Actuarial freedom from allograft degeneration was 81% \pm 3% and 71% \pm 5% at 10 and 16 years, respectively. Balloon valvuloplasty, stent placement, or both was performed in 7 patients, and in 5 of these, allograft replacement has not been required for up to 8 years after the intervention. Repeat intervention was required on 2 occasions in 2 patients.

Valve-related Morbidity

Valve-related morbidity is defined as AGF, ALF, endocarditis, and valve-related death. Actuarial freedom from valve-related morbidity was 80% \pm 3% and 63% \pm 6% at 10 and 16 years, respectively.

Discussion

The Ross operation has the advantages of a viable valve, excellent hemodynamics, freedom from hemolysis, no prosthetic valve sounds, growth in young children, and a low risk of endocarditis. However, the operation requires reconstruction of the right ventricular outflow tract with a nonviable valve and is a technically demanding operation with an increased operative risk and concern for the durability of the autograft valve. Debate continues about the most efficacious operative technique for implantation of the autograft valve, about patient selection, and about the most suitable replacement device for the transplanted pulmonary valve.

Operative Technique

The root replacement is the most versatile technique, allowing the surgeon to replace the aortic valve in patients of any age and to manage complicated left ventricular outflow tract obstructions. If the patient's pulmonary valve is normal, this technique is most likely to provide the patient with a competent autograft valve with minimal AGI at completion of the operation. The operation has an increased risk of intraoperative bleeding and a risk of malalignment of the coronary arteries at the time of implantation to the autograft root.

Our experience raises several technical and patient selection concerns. Autograft insufficiency was the most common cause of autograft reoperation. The most common cause of autograft insufficiency was late dilation of the autograft annulus, particularly in patients with AI as their primary lesion. We presently use aortic annulus fixation with synthetic material or glutaraldehyde-fixed pericardium in all older adolescents and adults whose BSA-standardized aortic annulus approaches a normal diameter. We reduce the aortic annulus if it is dilated. The only independent predictors of development of moderate–severe or severe AGI were increasing age at the time of the operation and AGI at completion of the operation and increasing follow-up time. Previous aortic valve replacement was protective.

Careful inspection of the pulmonary valve is essential before proceeding with a Ross operation. Use of a pulmonary valve with minor abnormalities will likely accelerate failure.

Ross operations that were performed in 5 patients whose pulmonary valves had minor abnormalities all required replacement of the autograft valve at 2.9 to 8.5 years, with a median of 4 years. Still, use of the valve is acceptable in some very young children or adolescents in whom other alternatives are less acceptable.

Our experience supports the use of the Ross operation in the management of patients with aortic valve endocarditis. Forty patients had endocarditis that led to aortic valve replacement, and in 24 patients it was active. In patients with active endocarditis, appropriate antibiotic therapy was completed after surgical intervention, and late endocarditis was identified in 5 patients, all related to recurrent intravenous drug use. The Ross operation was remarkably free of hospital-acquired endocarditis, which occurred in only 1 patient because of an infected central venous catheter.

Recent concern centers on autograft failure caused by autograft root dilation, especially in patients with a bicuspid aortic valve.⁷ In our series aortic valve morphology was not a risk factor for AGF by means of univariate or multivariate analysis.

Using echocardiographic standards for aortic sinus and root diameters, several authors have identified significant increases in autograft sinus and root diameters,⁸⁻¹⁰ whereas others have shown limited dilation after the first postoperative year.^{11,12} The use of echocardiographic standards for the aortic root or sinuses might not be appropriate. Many adults and children have autograft sinus or root diameters that exceed the accepted aortic diameters early, when the autograft root distends at systemic pressure. Our general linear mixed-model analyses of z-transformed aortic sinus or root diameters demonstrated that bicuspid aortic valve, repair of an ascending aortic aneurysm, grade 2 early postoperative AI, and history of a subaortic VSD were associated with more rapid increases in diameter during the first 12 months of follow-up. However, after 12 months, patients displaying these characteristics exhibit very gradual changes in diameter that do not differ from those of the overall group.

The optimal timing for autograft reoperation for dilation is unclear. Recently, Ergin and colleagues¹³ and Gleason and associates¹⁴ have suggested that elective operation on the dilated ascending aorta should be based on a ratio of observed to predicted diameter rather than the absolute size. They suggest a ratio of 1.5 as an indication for replacement of a degenerative aorta with or without AI or at the time of other cardiac surgery compared with a ratio of 1.3 for an elective operation in a patient with Marfan syndrome. Autograft root dissection is rare, with only 5 reported cases,^{1,5,15-19} and we have recently performed a reoperation on a patient with severe autograft insufficiency and a 5.3-cm autograft root and identified an unexpected chronic dissection. Autograft rupture has not been reported.

Accepting the suggestions of Ergin and colleagues¹³ and Gleason and associates¹⁴ and using the equations that Roman and coworkers²⁰ developed to predict diameters for the aortic

root and sinus of Valsalva from BSA, we identified 86 patients in our series with at least 1 ratio (echocardiographically measured diameter/predicted diameter) greater than 1.5. Forty-seven patients had 2 or more ratios greater than 1.5. The trajectories of these individual patients are shown in Figure E5. Although most demonstrate consistent ratios over time, a few have progressive increases in their ratios and might be candidates for elective replacement of their autograft root by a valve-sparing operation or a root replacement. These suggestions are in contrast to those of Luciano and Mazzucco.²¹

Our data suggest that male subjects with primary AI have an increased risk for autograft failure and might have an increased risk of reoperation, but they are not at a greater risk for autograft root dilation. The excellent survival and absence of thromboembolism or hemorrhage complications and a very low risk of endocarditis might warrant recommendation of a Ross operation, but the patient must be made aware of the likely increased risk of reoperation.

Increasing concern about the incidence of dilation of the autograft root has caused many surgeons to reconsider the subcoronary implant or the inclusion cylinder technique. The use of the subcoronary and inclusion techniques requires careful matching of the size of the autograft root to the aortic annulus size, the sinus diameter, and the sinotubular diameter of the aortic root. The autograft root is very distensible, and its size is probably best calculated from measurement of the diameter of the sinotubular ridge of the pulmonary root.²² The subcoronary and inclusion cylinder techniques cannot be used in patients who require replacement or reconstruction of the proximal aortic root or in patients who require a Ross-Konno procedure for management of left ventricular outflow tract obstruction. Also, infants and young children can rarely have a Ross operation as a subcoronary implant or as an inclusion cylinder because of the small size of the aortic annulus.

Reconstruction of the Right Ventricular Outflow Tract

Pulmonary allografts were our choice for reconstruction of the right ventricular outflow tract. We based allograft size on patient age and used an allograft that was larger than the predicted pulmonary valve size based on BSA. When possible, allografts from donors with the blood type of the recipient were used. Previous multivariate analysis has shown young donor age, later year of operation, and non-Ross operation as risk factors for allograft failure.²³ Raanani and associates²⁴ identified younger donor age, shorter duration of cryopreservation, and smaller allograft size as independent predictors of late allograft stenosis in 109 patients undergoing the Ross operation. Both of these studies suggest that an immune-mediated response can be associated with allograft failure. Accelerated allograft failure caused by an immune-mediated response has been demonstrated in aortic allografts²⁵ and pulmonary allografts in children.²⁶

Alternative approaches to the management of right ventricular outflow tract reconstruction have been introduced. Novick and colleagues²⁷ have had early good results with the use of the freestyle porcine aortic root in 11 patients undergoing the Ross operation. Purohit and coworkers²⁸ reported good early results in 20 patients undergoing the Ross operation using the Contegra bovine jugular vein conduit for right ventricular reconstruction. Results with both approaches are encouraging, but significant follow-up must be obtained before their adoption as an improvement over the allograft.

Conclusion

The Ross operation remains an excellent choice for the child or young adult requiring aortic valve replacement. It provides excellent survival and hemodynamics in most patients, with limited effect on lifestyle. Its only significant valve-related morbidity is the development of AGF or ALF requiring reoperation. Survival and valve-related morbidity in this series of Ross operations compared favorably with contemporary reported patient outcomes of aortic mechanical and stented bioprosthetic valves,^{29,30} although this comparison is limited by our inability to have complete echocardiographic follow-up.

The only clinical parameters that clearly affect autograft degeneration are male sex and a primary diagnosis of AI. Aortic annulus fixation and reduction, when indicated, appear to delay the occurrence of autograft failure and might reduce the incidence. The role of sinotubular junction fixation, advocated by some, was not addressed in this study. Autograft root dilation remains a concern and might limit the applicability of the root replacement. Presently accepted standards for replacement of a dilated degenerative ascending aorta might be too conservative for the autograft root. Allografts remain the gold standard for right ventricular reconstruction. However, the development of a viable and durable means of reconstruction of the right ventricular outflow tract is needed. Lifetime echocardiographic surveillance should be maintained on all patients.

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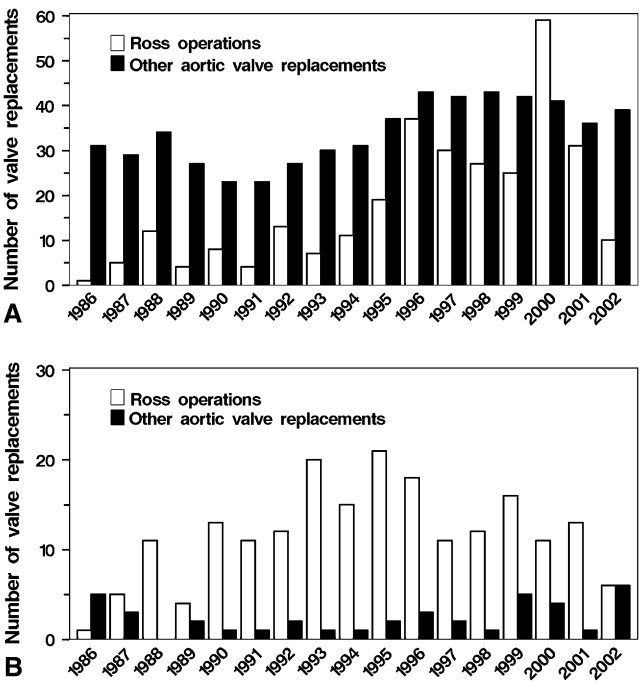


Figure E1. A, Aortic valve replacements in adults, Ross operations, and all others at University of Oklahoma Health Sciences Center, August 1986 through June 2002. B, Aortic valve replacements in children, Ross operations in children, and all others at University of Oklahoma Health Sciences Center, August 1986 through June 2002.

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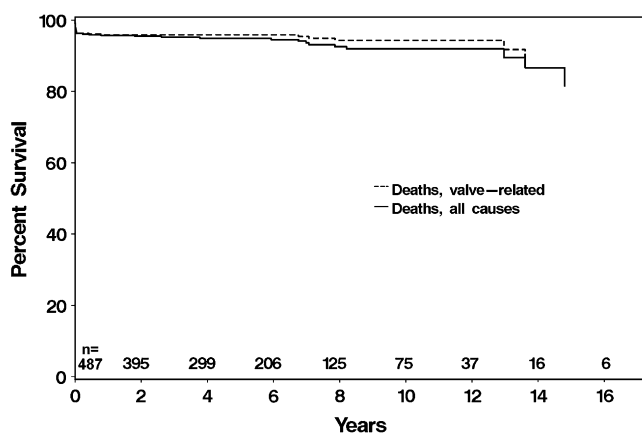


Figure E2. Actuarial survival from all causes and from valve-related deaths in 487 patients having a Ross operation, August 1986 through June 2002 as of August 2004.

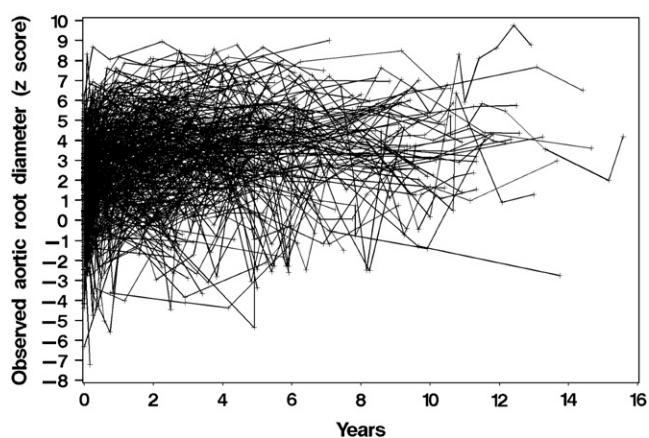


Figure E3. The z-transformed autograft sinus or root diameter of all 2147 echocardiograms obtained in 383 operative survivors over time. All calculated z scores are displayed (+) for each individual patient and connected by a line ending with the last follow-up. Significant variation occurred with the z scores of each individual patients over time related to variation in echocardiographic diameters measured and in some caused by increases in body surface area.

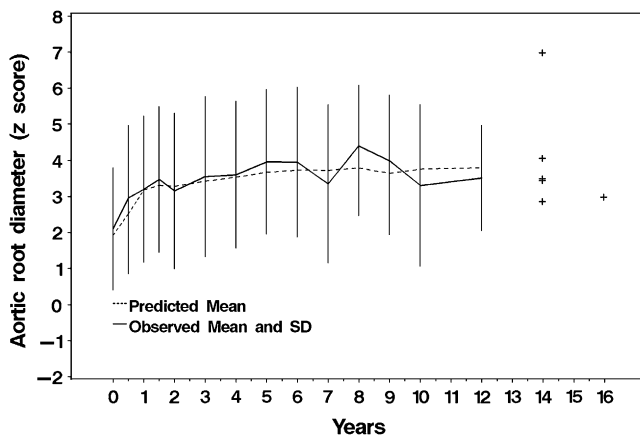


Figure E4. Mean observed and predicted z-transformed autograft sinus or root diameters. Observed mean diameters are calculated from individual patient means so that, for example, the mean at time zero represents all echocardiograms performed up to the third month. Means displayed for 0.5, 1, and 1.5 years include echocardiograms performed within 3 months of these time points. The mean reported at 2 years aggregates information from echocardiograms performed between 21 and 30 months after the operation. Means reported for 3 to 10 years of follow-up use all echocardiograms performed within 6 months. The mean reported for 12 years use all studies reported within 12 months. The small numbers available after 12 years of follow-up are shown individually. The predicted mean scores are derived from the general linear mixed model. The observed baseline (time = 0) mean z value of 1.97 ± 1.88 increases to a z value of 3.15 ± 2.18 at 1 year after the operation. Change thereafter is gradual.

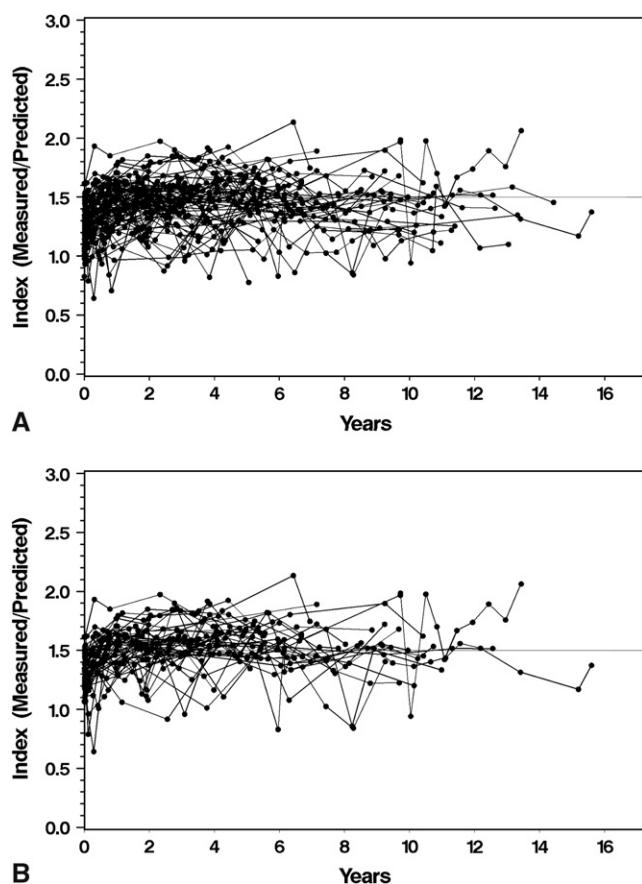


Figure E5. A, Individual plots over time of the calculated ratio of measured autograft diameter/predicted aortic diameter (by body surface area) for each patient (86) with a ratio of 1.5 or more. Consistent progressive increase in diameter was rarely identified. **B,** Individual plots over time of the calculated ratio of measured autograft diameter/predicted aortic diameter (body surface area) for each patient (45) with a ratio of 1.5 or greater on more than 1 echocardiogram. Some of these patients have shown a consistent increase in the value of their ratio and might be candidates for elective surgical intervention.